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IMMUNOSTIMULATORY NUCLEIC ACID MOLECULES

Related Application

This application is a divisional of U.S. Serial No. 08/960,774, filed October 30, 1997, NEW USPN 6,239,116,

5 which is a continuation-in-part of U.S. Serial No. 08/738,652, filed October 30, 1996, NOW USPN 6,267,646  
 pending, which is a continuation-in-part of U.S. Patent Application serial number 08/386,063, NEW USPN 6,194,383  
 filed February 7, 1995 currently pending, which is a continuation-in-part of U.S. Patent  
 Application 08/276,358, filed July 15, 1994 which is now abandoned, each of which are  
 incorporated herein by reference in their entirety.

Government

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 Health Grant No. R29-AR42556-01. The U.S. Government may have rights in the invention.

Field of the Invention

The present invention relates generally to oligonucleotides and more specifically to  
 15 oligonucleotides which have a sequence including at least one unmethylated CpG dinucleotide  
 which are immunostimulatory.

Background of the Invention

In the 1970s, several investigators reported the binding of high molecular weight DNA  
 to cell membranes (Lerner, R.A., *et al.* 1971. "Membrane-associated DNA in the cytoplasm  
 20 of diploid human lymphocytes." *Proc. Natl. Acad. Sci. USA* 68:1212; Agrawal, S.K., R.W.  
 Wagner, P.K. McAllister, and B. Rosenberg. 1975. "Cell-surface-associated nucleic acid in  
 tumorigenic cells made visible with platinum-pyrimidine complexes by electron microscopy."  
*Proc. Natl. Acad. Sci. USA* 72:928). In 1985, Bennett *et al.* presented the first evidence that  
 DNA binding to lymphocytes is similar to a ligand receptor interaction: binding is saturable,  
 25 competitive, and leads to DNA endocytosis and degradation into oligonucleotides (Bennett,  
 R.M., G.T. Gabor, and M.M. Merritt, 1985. "*J. Clin. Invest.* 76:2182). Like DNA,  
 oligodeoxyribonucleotides (ODNs) are able to enter cells in a saturable, sequence  
 independent, and temperature and energy dependent fashion (reviewed in Jaroszewski, J.W.,  
 and J.S. Cohen. 1991. "Cellular uptake of antisense oligodeoxynucleotides." *Advanced Drug*  
 30 *Deliver Reviews* 6:235; Akhtar, S., Y. Shoji, and R.L. Juliano. 1992. "Pharmaceutical aspects  
 of the biological stability and membrane transport characteristics of antisense  
 oligonucleotides." In: *Gene Regulation: Biology of Antisense RNA and DNA*. R.P.